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Section II (Remarks)

A. Summary of Amendment to the Claims

By the present Amendment, claims 1, 11, and 26 have been amended. Claims 2 and 14 were cancelled previously, and claims 22-25 have been withdrawn. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments. The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

B. Response to Claim Rejections Under 35 USC § 112

In the May 16, 2007 Office Action, claims 1, 3-13, 15-21 and 26-30 were rejected under 35 U.S.C. 112.

With regard to claims 1, 11, and 26, such claims were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner indicated that the recitation of "the non-elastomeric outer layer" could not be found in the written description of the application.

In response to such rejection, Applicants draw the Examiner's attention to paragraph [0057] of the present application, which states in the first sentence thereof:

To overcome various limitations of known interfaces, **preferred fluidic interfaces according to the present invention are gasketless and utilize non-elastomeric materials.**

Such disclosure follows substantial discussion in the Background section of the application of the undesirability of elastomeric materials, as indicated in the following excerpt from paragraph [0007] of the present application:

[E]lastomeric materials are subject to chemical degradation and swelling when exposed to chemicals typically employed in performing chromatography (particularly organic solvents such as acetonitrile, methanol, isopropyl alcohol, ethanol, ethyl acetate, and dimethyl sulfoxide). Any products of such degradation can be carried into an eluent stream and potentially interfere with sample analysis. Elastomeric materials also present sample carryover

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(contamination) problems in multi-use systems since such materials are often capable of retaining samples (e.g., through absorption or adsorption) used in one experimental run and then releasing such samples (e.g., through desorption) in a subsequent run. Moreover, elastomeric materials are subject to mechanical wear, thus conferring limited service life to components constructed with them.

Given Applicant's clear teaching of the undesirability of elastomeric materials for fluidic interfaces, and the use of "non-elastomeric materials" in preferred fluidic devices according to the present invention (e.g., paragraph [0057], withdrawal of the rejection of claims 1, 11, and 26 under 35 U.S.C. 112, first paragraph is warranted, and is respectfully requested.

With regard to claims 1, 3-13, 15-21, and 26-30, such claims were rejected under 35 U.S.C. 112, second paragraph, as being unclear for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner asserted that the adjectival modifier "substantially enclosed" as applied to "channel" (e.g., in claim 1, line 4, and further in claims 11 and 26) is unclear.

In response to such rejection, claims 1, 11, and 26 have been amended to substitute the term "covered" for "substantially enclosed" as applied to "internal microfluidic channel" (in claims 1 and 11) or "internal separation columns" (in claim 26). The adjectival term "substantially enclosed" as previously stated in the claims was intended to be synonymous with "covered" to distinguish *open* channels (*i.e.*, resembling trenches). Such distinction is apparent from paragraph [0039] of the application, which further supports the amendments to claims 1, 11, and 26, as reproduced below.

[0039] Traditionally, microfluidic devices have been fabricated from rigid materials such as silicon or glass substrates using surface micromachining techniques to define open channels and then affixing a cover to a channel- defining substrate to enclose the channels. There now exist a number of well-established techniques for fabricating microfluidic devices, including machining, micromachining (including, for example, photolithographic wet or dry etching), micromolding, LIGA, soft lithography, embossing, stamping, surface deposition, and/or combinations thereof to define apertures, channels or chambers in one or more surfaces of a material or that penetrate through a material

(Emphasis added.)

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The foregoing amendments to claims 1, 11, and 26 are fully supported by Applicant's disclosure, and eliminate any basis for rejecting such claims for lack of clarity under 35 U.S.C. 112, second paragraph. Accordingly, withdrawal of the rejections under 35 U.S.C. 112, second paragraph is warranted, and is respectfully requested.

C. Claim Rejection Under 35 USC § 103

The May 16, 2007 Office Action contained multiple rejections under 35 U.S.C. 103, including:

- A rejection of claims 1, 3-11, 15-21 and 26-30 under 35 U.S.C. 103 as being unpatentable for obviousness over U.S. Patent No. 7,060,227 to Staats ("Staats"); and
- A rejection of claims 12 and 13 under 35 U.S.C. 103 as being unpatentable for obviousness over Staats in view of U.S. Patent Application Publication No. 2004/0011648 to Paul et al. ("Paul"); 7,060,227 to Staats ("Staats").

Such rejections are traversed in application to the claims as amended herewith.

1. Law Regarding Obviousness

To support a rejection under 35 U.S.C. 103, the prior art reference(s) must teach all of the limitations of the claims. MPEP § 2143.03.

In considering a reference for its effect on patentability, the reference is required to be considered in its entirety, including portions of teach away from the invention under consideration. Simply stated, the prior art must be considered as a whole. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); MPEP § 2141.02. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Application of Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 448 (Fed. Cir. 1986), *cert. denied*, 484 U.S. 823 (1987).

According to the recent U.S. Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350, 550 U.S. ____ (April 30, 2007), the court did not disavow the previous "teaching, motivation or suggestion" or "TSM" test, but stated that such TSM test *should not be strictly*

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applied in determining obviousness. In connection with this point, the Supreme Court stated that:

“A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. ... [Rather], it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant art to combine the [prior art] elements in the manner claimed.” *KSR*, slip op. at 14.

It is fundamental to a proper rejection of claims under 35 U.S.C. § 103 that an examiner must present a convincing line of reasoning supporting the rejection. MPEP 2144 (“Sources of Rationale Supporting a Rejection Under 35 U.S.C. 103”), citing *Ex parte Clapp*, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985). The Supreme Court in *KSR* affirmed the validity of such approach, stating that **“there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.”**

In *KSR*, the Supreme Court further confirmed that references that teach away from the invention are evidence of the non-obviousness of a claimed invention, (*KSR*, slip op. at pp. 20-23) and reaffirmed the principle that a factfinder judging patentability “should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.”

2. Disclosure of Staats Relative to the Amended Claims

Staats teaches the assembly of microfluidic devices from a channel-defining substrate aligned, mated, and compressed against a cover or another substrate to form enclosed channels and other features. E.g., Staats Figures. 1-5, 13 & 18; col. 6, lines 60-62 (“when a second substrate is aligned with the first substrate, the microfluidic channels and other features are properly enclosed”). For example, Staats Figures. 1-3 illustrate various channel-defining substrates mated to covers, and Staats Figure 4-5 illustrate substrate-to-substrate interfaces with mating alignment protrusions, as illustrated below:

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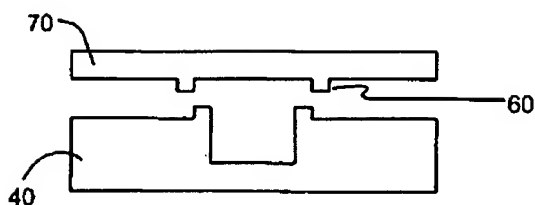


FIG. 4

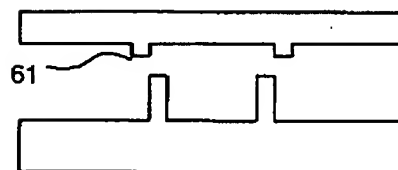


FIG. 5

Similarly to a substrate to cover interface, a **substrate to substrate interface** may include alignment features incorporated into the channel designs. Such features include ridges rising above the walls of the microfluidic channel, as **shown in FIG. 4 as an alignment protrusion 60**. These types of alignment protrusions preferably extend up to 100 .mu.m above the top surface plane of the substrate, and preferably up to 1000 .mu.m. The **corresponding protrusion on the bottom surface of the second substrate 70, the dimensions of the said protrusion is such that it fits tightly into the channel opening of the first substrate 40**. The channel depth with the second substrate 70 in place may be between 10 and 100 .mu.m, and preferably between 10 to 50 .mu.m. This alignment provides features such as access ports in a second substrate to align with features in the first substrate. FIG. 5 illustrates another embodiment in which the substrate 50 of FIG. 3 is mated with a second substrate 59 that has an alignment protrusion 61 extending therefrom. The dimensions of the protrusion 61 are such that the raised walls 54 are disposed between the protrusions 61.

Staats, col. 6, lines 20-39 (emphasis added).

Microfluidic device portions (e.g., lacking covers in at least FIGS. 6-10) with various protrusions and raised wall features defining open channels are illustrated in Staats Figures 6-13. Closed channels are formed in devices according to Staats only when one substrate is covered by another substrate or cover.

To provide a fluidic interface with a microfluidic device, Staats teaches the use of **raised capillaries** 130, 140. See, e.g., Staats Figures 12-13, as reproduced below:

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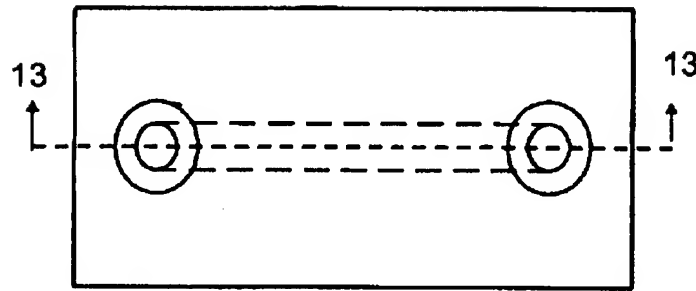


FIG. 12

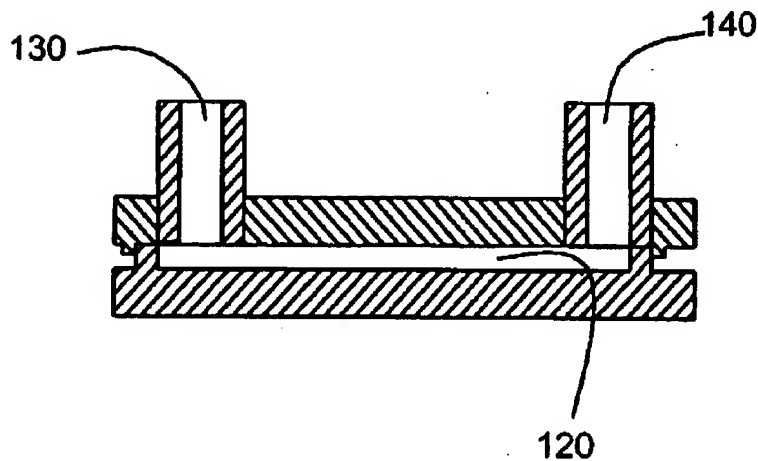


FIG. 13

In describing such Figures, Staats provides:

FIGS. 12 and 13 provide top and sectional views of an assembled microfluidic device with a single raised channel 120 with capillaries 130 and 140 attached to channel access ports which provide access to the channel for sample and buffer input or transport to a spectrometer for analysis.

Staats, col. 8, lines 32-36 (emphasis added).

Claim I of the instant application has been amended herewith to require, *inter alia*:

- a microfluidic device having a covered internal microfluidic channel and having an outer surface defining a first aperture;

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- a retractable element distinct and separate from the microfluidic device;
- the retractable element including a continuous raised feature that protrudes from a mating surface and surrounds a second aperture defined in the mating surface;
- a compression element adapted to depress the raised feature [of the retractable element] into the outer surface [of the microfluidic device].

Similarly, claim 11 of the instant application has been amended herewith to require, *inter alia*:

- a microfluidic device having a covered internal microfluidic channel and having an outer surface defining a first aperture;
- a retractable mating surface distinct and separate from the microfluidic device;
- the retractable mating surface including a protruding feature with a continuous wall that surrounds a second aperture;
- an actuator adapted to depress at least a portion of the protruding feature [of the retractable element] into an outer layer [of the microfluidic device].

Likewise, claim 26 of the instant application has been amended herewith to require, *inter alia*:

- a microfluidic device having a plurality of covered internal separation columns channels and having an outer surface defining a plurality of device apertures;
- a retractable seal plate distinct and separate from the microfluidic device;
- the retractable seal plate including a plurality of continuously raised features that protrude from a mating surface, with each raised feature surrounding a seal plate aperture;
- an actuator element adapted to depress at least a portion of the raised features [of the retractable seal plate] into the outer surface [of the microfluidic device].

No embodiment of Staats discloses a microfluidic device that has:

- (1) at least one covered internal (column or microfluidic channel) AND
- (2) a retractable seal plate distinct and separate from the microfluidic device, *let alone* any retractable seal plate having at least one continuously raised feature surrounding an aperture, or an actuator or compression element adapted to depress the seal plate into an outer surface of the microfluidic device.

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The Examiner asserts that Staats Figure 4 renders obvious the subject matter of the independent claims by showing a “retractable element” 70 that is ‘external to a channel-defining’ microfluidic device 40 [with the] ‘compressible raised feature’ 60 surrounding the ‘second aperture’ appear[ing] to be continuous.” May 16, 2007 Office Action, page 6.

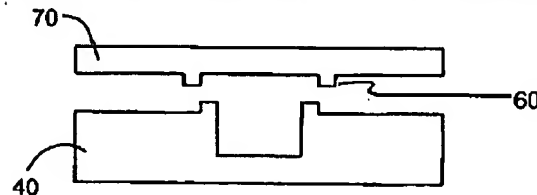


FIG. 4

Such disclosure of Staats CANNOT be equated with the subject matter of the amended claims, for at least the following reasons:

- no covered column or microfluidic channel can be formed by Staats until the second substrate 70 is mated with the first substrate 40 – thus, **the second substrate 70 is PART OF a microfluidic device, and CANNOT ALSO BE a “retractable (element or seal plate) distinct and separate from the microfluidic device;**
- Staats fails to teach any retractable (element or seal plate) that is distinct and separate from a microfluidic device and includes at least one continuously raised feature surrounding an aperture; and
- Staats fails to teach any (compression element or actuator) adapted to depress at least one raised feature into an outer surface of a microfluidic device to plastically deform the outer surface and provide sealing engagement between at least one aperture of the (compression element or actuator) and the microfluidic device.

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Based on the foregoing, Staats fails to "teach all of the limitations of the claims," as required by MPEP 2143.03 to support obviousness rejections of independent claims 1, 11, and 26. Because dependent claims inherently include all of the limitations of the claims on which they depend pursuant to 35 U.S.C. 112, all claims depending (whether directly or indirectly) from claims 1, 11, and 26 are likewise not obvious over Staats. Accordingly, withdrawal of the claim rejections under 35 U.S.C. 103 based on Staats is warranted, and is respectfully requested.

3. Disclosure of Paul in Application to the Amended Claims

Paul has been cited by the Examiner as disclosing "microfluidic flow devices which include: 'a wide variety of different micro-components' and can incorporate a high integrity seal that can withstand pressures in excess of 500 psi required for chromatographic separation and/or chemical processing.'" May 16, 2007 Office Action, page 5.

Paul discloses various flow devices including porous materials encapsulated within laminating materials to form channel enclosures. To provide fluid interfaces to such devices, Paul teaches the use of either "pigtailed capillaries" affixed by lamination (e.g., Paul, ¶ [0027] & FIG. 1) or "conventional HPLC fittings ... that are bonded by bonding material to an upper substrate" (e.g., Paul, ¶ [0032] & FIG. 4). FIGS 1 and 4 of Paul, which illustrate these alternative bonding methods, are reproduced below.

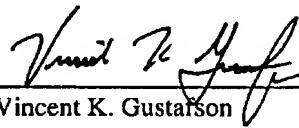
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remedy the deficiencies in the disclosure of Staats, such references in combination fail to support a rejection of Applicants' independent claims under 35 U.S.C. 103. Because dependent claims inherently include all of the limitations of the claims on which they depend pursuant to 35 U.S.C. 112, dependent claims 12-13 (which depend from claim 11) are likewise not obvious over Staats. Accordingly, withdrawal of the claim rejections under 35 U.S.C. 103 based on Staats and Paul is warranted, and is respectfully requested.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 1, 3-13, 15-21 and 26-30 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,



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